Factors influencing the successful treatment of infectious pulmonary tuberculosis

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Introduction

This study adopted a population-based approach to investigate the determinants impacting the effective management of infectious pulmonary pulmonary tuberculosis (PTB). It focused on all PTB patients residing in southern Taiwan, as documented in the tuberculosis registry spanning from January 1st to June 30th, 2018. The research entailed retrieving and analyzing the medical records of each patient from the hospitals where they were treated, covering a retrospective review period of 15 months following the confirmation of PTB diagnosis.

Method

The study conducted a population-based review of medical records in southern Taiwan, a region where the primary facility specializing in thoracic diseases, particularly tuberculosis (TB), is situated. Other hospitals and primary care providers offering TB treatment in the same area served as points of comparison. The study area encompassed Chiayi County, Chiayi City, Tainan County, and Tainan City. In compliance with Taiwanese law, all suspected and confirmed TB cases are required to be promptly reported to the national computerized registry maintained by the Taiwan Center for Disease Control (CDC). Reporting adherence has been enforced through policies such as a no-notification, no-reimbursement policy and a notification-for-free policy since 1997. The study team, comprising four registered nurses (each with at least six years of clinical experience), two head nurses (each with at least twelve years of clinical experience), and one pulmonologist, underwent extensive training to ensure the accuracy and consistency of data Validation. Site visits were conducted to review the medical records of all patients identified, with a subsequent 15-month-follow-up period after treatment initiation.

Healthcare institutions involved in the study comprised a chest hospital, two academic medical centers, 11 regional hospitals, and 15 district hospitals, alongside primary practitioners, all playing roles in tuberculosis (TB) case reporting and treatment in Taiwan. In Taiwan's governmental classification, medical centers are comprehensive facilities with over 500 acute-care beds, while regional hospitals have at least 250 acute-care beds and offer various medical specialties, and district hospitals provide primary care services with in-patient capabilities.

Infectious pulmonary tuberculosis (PTB) is diagnosed through sputum culture confirmation, positive sputum smear tests for acid-fast bacilli (AFB), radiology signs, or clinical diagnosis.

Directly observed treatment (DOT) involves a non-family member healthcare worker supervising patient ingestion of anti-TB medications for the first two months. Taiwan follows WHO-recommended TB treatment regimens regardless of DOT implementation.

Treatment success is defined as patient cure or completion of treatment, with cure indicating negative bacteriology results at treatment completion.

Ethical approval was obtained from the Taiwan CDC, with confidentiality agreements signed by all the study personnel.

Data Analysis

The study employed chi-square tests in bivariate analyses to compare proportions of dichotomous and categorical variables, identifying potential predictors of successful treatment. Subsequently, multivariate logistic regression analyses were conducted on predictors with $P < 0.10$ from bivariate analyses. Initially, a full model encompassing all potential predictors was constructed, followed by a forward substitution model building procedure to create a reduced model with statistically significant predictors. Odds ratios (ORs) and 95% confidence intervals (CIs) of risk variables on binary outcomes were calculated. SPSS 10.0 software was used for all analyses, with tests conducted at a two-tailed significance level of 0.05.

Table 1 Characteristics of 399 patients with PTB and univariate analyses of potential predictors of successful treatment

Characteristics	Patients n (%)	Successful treatment* n (%)	P Value+
Sex			0.392
Male	293 (73.4)	198 (67.6)	
Female	106 (26.6)	77 (72.7)	
Patients with comorbidities			0.018
No comorbidity	143 (35.9)	109 (76.2)	
With comorbidity	255 (64.1)	165 (64.7)	
Unknown	1	1 (100)	
CXR			0.015
Cavitations	127 (31.9)	98 (77.2)	
No cavitation	271 (681.)	176 (64.9)	
Unknown	1	1 (100)	
Previous TB Treatment			0.815
Yes	22 (5.8)	16 (72.7)	
No	360 (94.2)	246 (68.3)	
Unknown	17	12 (70.6)	
DOT			0.002
Yes	250 (63.1)	186 (74.4)	
No	146 (36.9)	86 (58.9)	
Unknown	3	3 (100)	
Diagnostic and treating physicians			<0.001
Pulmonologist	298 (74.7)	221 (74.2)	

Non-pulmonologist	102 (25.6)	55 (53.9)	
Health-care institutions			<0.001
Medical center	105 (26.3)	68 (64.8)	
Regional Hospital	144 (36.1)	92 (63.9)	
District hospital and primary practitioners	98 (24.6)	66 (67.3)	
Chest specialty hospital	52 (13.0)	49 (94.2)	
Total	399 (100)	275 (68.9)	

*15- month follow-up after start of treatment.

+X^2 test.

PTB = pulmonary tuberculosis; CXR= chest X-ray; TB= tuberculosis; DOT= directly observed treatment

Question 1

Describe the roles biostatistics serves in the discipline of public health?

Biostatistics plays several crucial roles in the discipline of public health:

1. **Data Collection and Analysis**- Biostatistics involves the collection, organization, and analysis of data related to public health issues. This includes designing surveys, experiments, and observational studies to gather relevant information about health outcomes, risk factors, and interventions.

2. **Descriptive Statistics**- Biostatistics helps in summarizing and describing data using measures such as mean, median, mode, standard deviation, and percentiles. These statistics provide insights into the distribution of health-related variables within populations.

3. I**nferential Statistics**- Biostatistics facilitates making inferences or generalizations about populations based on sample data. Techniques such as hypothesis testing, confidence intervals, and regression analysis allow public health researchers to draw conclusions about the effectiveness of interventions, the presence of associations between variables, and the impact of risk factors on health outcomes.

4. **Study Design**- Biostatistics guides the design of research studies in public health, ensuring that studies are appropriately powered, minimize bias, and address potential confounding variables. This involves determining sample sizes, randomization procedures, and control measures to enhance the validity and reliability of study findings.

5. **Public Health Surveillance**- Biostatistics is essential for monitoring the health status of populations through surveillance systems. By analyzing trends in disease incidence, prevalence, and mortality rates, biostatisticians can identify emerging health threats, evaluate the effectiveness of public health programs, and inform policy decisions.

6. **Risk Assessment and Prediction**- Biostatisticians help assess the risk factors associated with various health outcomes and predict the likelihood of future events. Techniques such as logistic regression, survival analysis, and risk modeling enable public health practitioners to identify high-risk populations, prioritize interventions, and allocate resources effectively.

7. **Evidence-Based Decision Making**- Biostatisticians provides the quantitative framework for evidence-based decision making in public health. By synthesizing data from multiple studies through meta-analysis and systematic reviews, biostatisticians helps policy makers, healthcare providers, and public health professionals make informed decisions about interventions, policies, and resources allocation strategies.

Overall, biostatistics serves as a fundamental tool for generating knowledge, informing public health practice, and ultimately improving the health outcomes of populations.

Question 2

What proportion of patients was successfully treated?

To determine the proportion of patients who were successfully treated, we can refer to the "Successful Treatment" column in Table 1.

From the table:

Total number of patients = 399

Number of patients successfully treated = 275

Proportion of patients successfully treated = (Number of patients successfully treated / Total number of patients) x 100

Proportion of patients successfully treated = (275 / 399) x 100 = 68.92%

So, approximately 68.9% of patients were successfully treated.

Question 3

Calculate a 95% Confidence Interval (CI) for the true population proportion with successful treatment. Hint: The SE of p is the square root of (pq) / n

To calculate the 95% Confidence Interval (CI) for the true population proportion with successful treatment, we will use formula:

Confidence Interval = Sample Proportion $\pm$ Margin of error

Where:

Sample proportion ($\widehat{p}$) is the proportion of patients successfully treated.

Margin of error is determined by z-value corresponding to the desired confidence level and the standard error of the sample proportion.

Firstly, lets calculate the standard error (SE) of the Sample proportion ($\widehat{p}$):

$$\text{SE} = \sqrt{\frac{\widehat{p}((1-\widehat{p})}{n}}$$

Given:

Sample proportion ($\widehat{p}$) = 0.689 (From the proportion of successful treatment)

Sample size (n) = 399

$$\text{SE} = \sqrt{\frac{0.689\ x\ (1-0.689)}{399}}$$

$$SE = \sqrt{\frac{0.689\ x\ (0.311)}{399}}$$

$$SE = \sqrt{\frac{0.214179}{399}}$$

$$SE = \sqrt{0.000536}$$

SE = 0.0231

Next, we'll determine the margin of error using the z-value for a 95% confidence interval, which corresponds to z = SE

Margin of Error = z x SE

Margin of Error = 1.96 x 0.0231

Margin of Error = 0.04528

Now, we can calculate the confidence interval:

Confidence Interval = 0.689 ± 0.04528

Confidence Interval = (0.6437 , 0.7343)

Therefore, the 95% confidence interval for the true population proportion with successful treatment is approximately (0.6437 , 0.7343).

Question 4

Write a sentence that describes the meaning of the 95% CI.

The 95% confidence interval (CI) represents the range of values within which we are 95% confident that the true population proportion of patients with successful treatment lies, based on the observed sample data and statistical analysis.

Question 5

Using the information from Table 1, construct a 2x2 table to test the association between DOT status and successful treatment.

Observed Treatment Success

DOT	Yes	No	Total
Yes	Yes	No	250
No			146
Unknown			003
Total	275	124	399

Here is a 2x2 Table constructed to test the association between DOT status and successful treatment.

Observed Treatment Success

DOT	Yes	No	Total
Yes	186	64	250
No	86	60	146
Unknown	3	0	003
Total	275	124	399

In the table above:

For patients receiving DOT (DOT Status = Yes). 186 were successfully treated, and 64 were unsuccessfully treated.

For patients not receiving DOT (DOT Status = No), 86 were successfully treated, and 60 were unsuccessfully treated.

For patients with unknown DOT Status, 3 were successfully treated, and none were unsuccessfully treated.

We can perform statistical tests, such as chi-squared test, to determine if there is a significant association between DOT Status and successful treatment.

Question 6

Generate the expected values for the empty cells below. Hint: the expected value is the row total x column total divided by the grand (overall) total

Expected Treatment Success Values

DOT	Yes	No	Total
Yes	Yes	No	250
No			146
Unknown			003
Total	275	124	399

To calculate the expected values for the empty cells, we'll use the formula:

Expected Value = (Row Total x Column Total) / Grand Total

Here are the calculations:

For the cell where DOT is "Yes" and Treatment Success is "Yes":

Expected Value = (Row Total for "Yes" in DOT) * (Column Total for "Yes" in Treatment Success) / Grand Total

= (250 * 275) / 399

≈ 172.30

For the cell where DOT is "Yes" and Treatment Success is "No":

Expected Value = (Row Total for "Yes" in DOT) * (Column Total for "No" in Treatment Success) / Grand Total

= (250 * 124) / 399

≈ 77.69

For the cell where DOT is "No" and Treatment Success is "Yes":

Expected Value = (Row Total for "No" in DOT) * (Column Total for "Yes" in Treatment Success) / Grand Total

= (146 * 275) / 399

≈ 100.63

For the cell where DOT is "No" and Treatment Success is "No":

Expected Value = (Row Total for "No" in DOT) * (Column Total for "No" in Treatment Success) / Grand Total

= (146 * 124) / 399

≈ 45.37

For the cell where DOT is "Unknown" and Treatment Success is "Yes":

Expected Value = (Row Total for "Unknown" in DOT) * (Column Total for "Yes" in Treatment Success) / Grand Total

= (3 * 275) / 399

≈ 2.07

For the cell where DOT is "Unknown" and Treatment Success is "No":

Expected Value = (Row Total for "Unknown" in DOT) * (Column Total for "No" in Treatment Success) / Grand Total

= (3 * 124) / 399

≈ 0.93

Expected Treatment Success Values

DOT	Yes	No	Total
Yes	172.30	77.69	250
No	100.63	45.37	146
Unknown	2.07	0.93	003
Total	275	124	399

The table above shows the calculated expected values.

Question 7

Given these expected values, is the chi-square test an appropriate statistical test?

To determine whether the chi-square test is appropriate for analyzing these expected values, we need to ensure that certain conditions are met. The chi-square test is typically used for categorical data analysis when certain assumptions are satisfied:

> **Independence**: Each observation must be independent of the others. In this case, it's assumed that the responses from different individuals are independent.
>
> **Sample Size**: Each expected cell count should be at least 5. This is a general rule of thumb to ensure the validity of the chi-square test.

Let's calculate the expected cell counts:

For "Yes":

- Expected count for "Yes,Yes" = (250 * 275) / 399 = 172.30
- Expected count for "Yes,No" = (250 * 124) / 399 = 77.69
- Expected count for "Yes,Unknown" = (250 * 3) / 399 = 1.88

For "No":

- Expected count for "No,Yes" = (146 * 275) / 399 = 100.63
- Expected count for "No,No" = (146 * 124) / 399 = 45.37
- Expected count for "No,Unknown" = (146 * 3) / 399 = 1.10

For "Unknown":

- Expected count for "Unknown,Yes" = (3 * 275) / 399 = 2.07
- Expected count for "Unknown,No" = (3 * 124) / 399 = 0.93
- Expected count for "Unknown,Unknown" = (3 * 3) / 399 = 0.02

All expected counts are above 5, which satisfies the sample size condition.

Therefore, based on the provided expected values, the chi-square test seems to be appropriate for analyzing the data, assuming independence of observations.

Question 8

Which of the following would be an appropriate approach to the analysis of these data?

Yes/No A. Fisher’s exact test using all data

Yes/No B. Chi-square or Fisher’s exact test after deleting unknowns

Both Fisher's exact test and the Chi-square test can be appropriate approaches for analyzing categorical data like this. However, the choice between the two depends on certain factors.

Fisher's exact test is typically used when sample sizes are small (especially when any expected cell count is below 5) or when the data violates the assumptions of the Chi-square test. It is exact, meaning it calculates the probability of obtaining the observed distribution or one more extreme, given the marginal totals.

The Chi-square test is more commonly used and is appropriate when sample sizes are large and the expected cell counts are not too low (typically, all expected cell counts should be at least 5). It is a good test for assessing the independence of categorical variables.

In this scenario, you have a small expected count in the "Unknown" category. So, one option would be to remove this category and conduct either a Chi-square or Fisher's exact test on the remaining data. However, before removing any data, it's important to understand the implications and potential biases it may introduce.

Given the small expected count in the "Unknown" category, using Fisher's exact test with all the data would be appropriate. So, the answer would be:

A. Yes - Fisher’s exact test using all data

Solutions and Suggestions

Directly Observed Treatment (DOT):

- **Strengthen DOT implementation**: Ensure that all PTB patients, especially those identified as requiring DOT, receive proper supervision during medication intake for the first 2 months of treatment. This may involve training additional health workers or volunteers to assist with DOT, especially in areas where resources are limited.

- **Patient education and engagement**: Educate patients on the importance of adhering to their treatment regimen, particularly during the initial phase when DOT is required. Encourage patients to actively participate in their treatment and address any concerns or barriers they may face in adhering to DOT.

Diagnostic and treating physicians:

- **Ensure adequate training and resources for non-pulmonologist physicians**: Provide additional training and support for non-pulmonologist physicians involved in the diagnosis and treatment of PTB patients. This may include workshops, continuing education programs, and access to expert consultation to improve their knowledge and skills in managing PTB cases effectively.

- **Collaboration and referral systems**: Foster collaboration between pulmonologists and non-pulmonologist physicians to ensure seamless coordination of care for PTB patients. Establish clear referral pathways for cases requiring specialized care or management beyond the scope of non-pulmonologist physicians.

Health-care institutions:

- **Resource allocation and capacity building**: Allocate resources and support to health-care institutions based on their capacity to provide TB care. Prioritize funding, staffing, and infrastructure improvements for institutions serving high-burden areas or populations with limited access to care.

- **Strengthening primary care services**: Enhance the capacity of district hospitals and primary practitioners to provide comprehensive TB care, including diagnosis, treatment, and patient support services. This may involve training primary care providers in TB management, providing access to diagnostic tools and medications, and integrating TB services into existing primary care programs.

Patient characteristics (sex, comorbidities, CXR findings, previous TB treatment):

- **Individualized treatment and support**: Tailor treatment plans and support services based on the specific needs and characteristics of PTB patients. Provide targeted interventions for vulnerable populations, such as those with comorbidities or previous TB treatment, to improve treatment outcomes and reduce barriers to care.

- **Regular monitoring and follow-up**: Implement a system for regular monitoring and follow-up of PTB patients throughout their treatment journey. This may involve establishing patient registries, conducting home visits or telehealth consultations, and providing ongoing support and education to promote treatment adherence and address any challenges or concerns.

By addressing these key factors through targeted interventions and system-level improvements, it is possible to enhance the success of PTB treatment and improve patient outcomes in southern Taiwan. This approach requires a coordinated effort involving healthcare providers, policymakers, and community stakeholders to implement and sustain effective TB control measures.

Limitations

Addressing the problems associated with the successful treatment of infectious pulmonary tuberculosis (PTB) involves overcoming several challenges and limitations. Here are some expected challenges and limitations:

Resource Constraints:

- Limited healthcare infrastructure and personnel may hinder the effective delivery of directly observed treatment (DOT) and comprehensive care to PTB patients.
- Insufficient funding for TB control programs may restrict the implementation of interventions aimed at improving treatment success rates.

Access to Care:

- Geographical barriers and disparities in healthcare access may prevent some PTB patients, particularly those in rural or remote areas, from receiving timely diagnosis and treatment.
- Socioeconomic factors such as poverty, lack of transportation, and stigma associated with TB may further impede access to care for certain populations.

Health System Capacity:

- Overburdened healthcare systems may struggle to accommodate the increasing demand for TB diagnosis, treatment, and follow-up care, leading to delays and suboptimal outcomes.
- Limited availability of trained healthcare providers, particularly pulmonologists and specialized TB nurses, may compromise the quality and consistency of care provided to PTB patients.

Patient Adherence and Engagement:

- Adherence to treatment regimens, especially during the initial phase requiring DOT, can be challenging due to factors such as medication side effects, stigma, and competing priorities.
- Patient education and support programs may be underutilized or ineffective in promoting treatment adherence and addressing patient concerns and misconceptions about TB.

Diagnostic Challenges:

- Delays or inaccuracies in TB diagnosis, including the identification of drug-resistant strains, may result in suboptimal treatment outcomes and increased transmission within the community.
- Limited access to diagnostic tools, such as GeneXpert testing for rapid TB detection and drug susceptibility testing, may hinder timely and accurate diagnosis.

Data Quality and Surveillance:

- Incomplete or inaccurate reporting of TB cases to the national registry may compromise the validity and reliability of epidemiological data used for monitoring treatment outcomes and guiding public health interventions.
- Challenges in data collection and management, including discrepancies in medical record documentation and follow-up procedures, may affect the completeness and consistency of data analyzed for research purposes.

Stakeholder Collaboration and Coordination:

- Fragmentation of TB control efforts across different healthcare institutions and stakeholders may hinder coordination and collaboration in implementing evidence-based interventions and addressing systemic barriers to treatment success.
- Inadequate communication and engagement between healthcare providers, policymakers, and community organizations may limit the effectiveness of comprehensive TB control strategies and advocacy efforts.

Cultural and Social Context:

- Cultural beliefs, practices, and social norms surrounding TB may influence patient behavior, healthcare-seeking patterns, and treatment acceptance, posing challenges to culturally competent care delivery and community engagement.
- Addressing social determinants of health, such as poverty, housing instability, and substance abuse, may require multisectoral approaches and community-based interventions to support PTB patients throughout their treatment journey.

Addressing these challenges and limitations requires a multifaceted approach that involves strengthening healthcare systems, promoting patient-centered care, enhancing community engagement, and addressing social and structural determinants of health. Collaboration between policymakers, healthcare providers, community organizations, and affected individuals is essential to overcoming these barriers and achieving improved treatment outcomes for PTB patients in southern Taiwan.

Recommendations

Here are recommendations for addressing factors influencing the successful treatment of infectious pulmonary tuberculosis (PTB) in southern Taiwan, along with future prevention plans:

Enhance Access to Care:

- Establish mobile TB clinics or outreach programs to provide TB diagnosis, treatment, and follow-up care in underserved areas, particularly rural and remote regions.
- Strengthen referral networks and collaboration between healthcare institutions to ensure timely access to specialized TB care, including chest specialty hospitals and academic medical centers.

Improve Patient Adherence and Engagement:

- Implement patient education and counseling programs to address misconceptions, stigma, and barriers to treatment adherence.
- Offer incentives or support services, such as transportation vouchers or nutritional assistance, to facilitate patient participation in directly observed treatment (DOT) and clinic visits.

Enhance Diagnostic Capacity:

- Invest in the procurement and deployment of advanced diagnostic technologies, such as GeneXpert testing for rapid TB detection and drug susceptibility testing, to expedite diagnosis and inform appropriate treatment regimens.
- Provide training and support for healthcare providers in the accurate interpretation of diagnostic tests and radiological findings for TB diagnosis and management.

Strengthen Healthcare System Capacity:

- Increase the recruitment and retention of skilled healthcare professionals, including pulmonologists, specialized nurses, and laboratory technicians, to support TB care delivery and surveillance.
- Invest in infrastructure upgrades and equipment maintenance to ensure the efficient operation of TB diagnostic and treatment facilities, including laboratory services and medication supply chains.

Promote Data Quality and Surveillance:

- Implement electronic medical record systems and standardized reporting protocols to enhance the accuracy and completeness of TB case reporting and surveillance.

- Provide training and technical support for healthcare personnel involved in data collection, entry, and analysis to improve data quality and reliability for monitoring treatment outcomes and epidemiological trends.

Community Engagement and Advocacy:

- Foster partnerships with community organizations, advocacy groups, and local leaders to raise awareness about TB prevention, diagnosis, and treatment.
- Empower affected individuals and communities to participate in TB control efforts through education, peer support, and involvement in decision-making processes.

Future Prevention Plan:

- Implement TB prevention strategies focusing on early detection, contact tracing, and infection control measures to interrupt transmission chains and prevent the spread of TB within communities.
- Strengthen TB surveillance systems to monitor trends in TB incidence, drug resistance, and treatment outcomes, enabling the timely implementation of targeted interventions.

- Promote research and innovation in TB diagnostics, therapeutics, and vaccines to accelerate progress towards TB elimination goals and reduce the burden of TB-related morbidity and mortality in southern Taiwan.

By implementing these recommendations and investing in future prevention efforts, southern Taiwan can enhance the success of PTB treatment, improve patient outcomes, and work towards the ultimate goal of TB elimination.

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